Gefitinib

Cat. No.: HY-50895

CAS No.: 184475-35-2

Molecular Formula: $C_{22}H_{24}ClFN_4O_3$

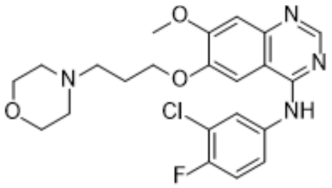
Molecular Weight: 446.9

Target: EGFR; Autophagy; Apoptosis

Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (223.76 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2376 mL	11.1882 mL	22.3764 mL
5 mM	0.4475 mL	2.2376 mL	4.4753 mL
10 mM	0.2238 mL	1.1188 mL	2.2376 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: corn oil
   Solubility: 5 mg/mL (11.19 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.65 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.65 mM); Clear solution
5. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: 0.5 mg/mL (1.12 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Gefitinib (ZD1839) is a potent, selective and orally active EGFR tyrosine kinase inhibitor with an IC_{50} of 33 nM. Gefitinib selectively inhibits EGF-stimulated tumor cell growth (IC_{50} of 54 nM) and that blocks EGF-stimulated EGFR autophosphorylation in tumor cells. Gefitinib also induces autophagy and cell apoptosis, which can be used for cancer

	related research, such as Lung cancer and breast cancer [1][2][5].
IC_{50} & Target	EGFR
In Vitro	Gefitinib (0.01-0.1 μM, 72 h) results in increased phosphotyrosine load of the receptor, increased signalling to ERK and stimulation of proliferation and anchorage-independent growth[2]. Gefitinib (1-2 μM, 72 h) significantly decreases EGFRvIII phosphotyrosine load, EGFRvIII-mediated proliferation and anchorage-independent growth[2]. Gefitinib (0.62 μM, 24-72 h) inhibits IL-13-induced M2-like polarization of RAW 264.7 cells through the STAT6-dependent signaling pathway[3]. Gefitinib (0.62 μM, 72 h) inhibits M2-like macrophage-promoted invasion and migration[3]. Gefitinib (0-10 μM, 72 h) induces apoptosis (induction of BIM protein) in NSCLC Cell Lines (H3255 and HCC827 cells)[4]. Gefitinib (100 nM, 24 h) suppresses macropinocytosis and increases the cellular uptake of extracellular vesicles(EVs) in HCC827 and A549 cells[6]. Gefitinib (1.5-60 μM, 48 h) increases inhibition of proliferation in $H358^R$ and $A549^R$ cells (Cisplatin-resistant wtEGFR NSCLC cell lines)[7]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	NR6wtEGFR, NR6W and NR6M
Concentration:	1, 10, 100 μM
Incubation Time:	5 h
Result:	Inhibited EGFR tyrosine phosphorylations.

Cell Migration Assay [3]

Cell Line:	LLCs cell
Concentration:	0.62 μM
Incubation Time:	72 h
Result:	Abrogated M2-like macrophage promoted invasion and migration of LLCs.

In Vivo	Gefitinib (Oral administration, 75 mg/kg/d, 21 days) inhibits the M2-like polarization of macrophages in LLC mice metastasis model[3]. Gefitinib (Oral administration, 75 mg/kg for the initial week, daily for 5 consecutive days per week) eliminates phosphorylation of HER2 and HER3 and signaling through MAPK and Akt in lobular hyperplasias and carcinomas, increases MAPK activity and cytokine production in splenocytes and lymph nodes[5].Gefitinib (Oral gavage, 150 mg/kg, daily) enhances the anti-tumor effect of Cisplatin in $H358^R$ xenograft[7]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	LLC mice metastasis model[3]
Dosage:	75 mg/kg/d, for 21 days.
Administration:	Oral administration
Result:	Reduced the number of lung metastasis nodules, down-regulated the expression of M2 marker genes and the percentages $CD206^+$ and $CD68^+$ macrophages in tumor tissues.

Animal Model:	BALB-NeuT transgenic mouse model[5]
Dosage:	75 mg/kg for the initial week, and increased by 15 mg/kg every other week, daily for 5 consecutive days per week, followed by 2 days without treatment and repeated for 8–9 weeks.
Administration:	Oral administration
Result:	Reduced tumor multiplicity from 9.6 to 0.58 (83%), and reduced the number and size of lobules and lobular nodules in treated mice.

CUSTOMER VALIDATION

- Cancer Cell. 2018 Jun 11;33(6):1061-1077.e6.
- Cell Res. 2021 Jun;31(6):631-648.
- Cell Res. 2020 Oct;30(10):833-853.
- Signal Transduct Target Ther. 2019 Dec 13;4:60.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.

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REFERENCES

[1]. Pedersen MW, et al. Differential response to gefitinib of cells expressing normal EGFR and the mutant EGFRvIII. Br J Cancer. 2005 Oct 17;93(8):915-23.

[2]. Muhammad Tariq, et al. Gefitinib inhibits M2-like polarization of tumor-associated macrophages in Lewis lung cancer by targeting the STAT6 signaling pathway. Acta Pharmacol Sin. 2017 Nov;38(11):1501-1511.

[3]. Mark S Cragg, et al. Gefitinib-induced killing of NSCLC cell lines expressing mutant EGFR requires BIM and can be enhanced by BH3 mimetics. PLoS Med. 2007 Oct;4(10):1681-89; discussion 1690.

[4]. Marie P Piechocki, et al. Gefitinib prevents cancer progression in mice expressing the activated rat HER2/neu. Int J Cancer. 2008 Apr 15;122(8):1722-9.

[5]. Tomoya Takenaka, et al. Effects of gefitinib treatment on cellular uptake of extracellular vesicles in EGFR-mutant non-small cell lung cancer cells. Int J Pharm. 2019 Dec 15;572:118762.

[6]. Amin Li, et al. Gefitinib sensitization of cisplatin-resistant wild-type EGFR non-small cell lung cancer cells. J Cancer Res Clin Oncol. 2020 Jul;146(7):1737-1749.

[7]. Wakeling AE, et al. ZD1839: an orally active inhibitor of epidermal growth factor signaling with potential for cancer therapy. Cancer Res. 2002 Oct 15;62(20):5749-54.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA